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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,936	03/10/2004	Martial G. Bourassa	5197-102 US	3284

7590 03/23/2007

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,936	BOURASSA ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) 8-22 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☒ Claim(s) 1 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 6/7/04;8/20/04;8/15/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restrictions

Applicant's election with traverse of claims **1-7** in the reply filed on 10/12/06 is acknowledged. Claims **8-22** are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/10/06. The traversal is on the ground(s) that the methods of groups II and III are searchable with group I. This is not found persuasive because administering a beta-blocker as in group II and an angiotensin II receptor as in group III are directed to a different modes of actions. As stated in the restriction requirement inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 07, 2004, August 20, 2004 and August 15, 2005 has been received and acknowledged. A duplicate copy of the Vermes et al. Circulation 2003;107;1291-1296 is noted, only one is acknowledged.

Claim Objections

Claim 1 is objected to because of the following informalities: The abbreviation ACE should be spelled out when first used. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the incidence of diabetes mellitus in a subject with chronic heart failure comprising administering a therapeutically effective amount of an agiotensin-converting enzyme inhibitor, does not reasonably provide enablement for preventing. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of preventing the incidence of diabetes mellitus in a subject with chronic heart failure comprising administering a therapeutically effective amount of an agiotensin-converting enzyme inhibitor (ACE). The nature of the invention is extremely complex in that it encompasses the actual prevention of the incidence of diabetes mellitus such that the subject treated with an ACE inhibitor does not ever suffer from the incidence of mellitus. Please note when prevention is suppose to never occur in the first instant. Early intervention with ACE inhibitors has been demonstrated to slow the progression of left ventricular enlargement and reduce morbidity and mortality. However, It is likely that selective administration of these drugs would be effective in responsive patient populations, but the criteria for identifying these populations are not yet available. Heart failure is a progressive and lethal disease if left untreated. Even with existing therapy, the mortality rate remains high, and the quality of life and morbidity are significantly impaired. (see enclosed reference (JAY N. COHN, M.D., University of Minnesota Medical School, Minneapolis, Minnesota) vol. 57(8) 1998. Next, diabetes mellitus a Type 1, also known as insulin dependent diabetes, occurs mainly in childhood or early adolescence and requires daily insulin injections for survival. The most common form is caused by the destruction of beta cells in the pancreas by the auto-immune

system, leaving the pancreas unable to produce insulin. So how is this incident prevented?

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. (see above)

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent obesity is minimal. All of the guidance provided by the specification is directed towards treatment rather than prevention of obesity.

Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than prevention. Page 7 The effect of enalapril in a subgroup of patients known to be at high risk for diabetes, ie, those with impaired FPG at baseline, found only 1 patient developed diabetes in the enalapril group compared with 12 patients in the placebo group, which represent an absolute risk reduction of 45% (Table 3) of the specification discussed decrease. Thus reduction is not prevention.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prevention early intervention with ACE inhibitors has been demonstrated to slow the progression of left ventricular enlargement and reduce morbidity and mortality. However, It is likely that selective administration of these drugs would be effective in responsive patient populations, but the criteria for identifying these populations are not yet available. Heart failure is a progressive and lethal disease if left untreated.

Even with existing therapy, the mortality rate remains high, and the quality of life and morbidity are significantly impaired. (see enclosed reference (JAY N. COHN, M.D., University of Minnesota Medical School, Minneapolis, Minnesota) vol. 57(8) 1998.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Vermes et al. Circulation 2003;107;1291-1296 Feb. 17 (submitted by Applicant).

The above reference teaches with regards to instant claim 1 the effect of ACE inhibition on the development of diabetes in heart failure population-thus inclusive of chronic heart failure administering an Ace inhibitor enalapril as in claims 1, 5 and 7 (see rt. col. first para. highlighted) wherein the Ace inhibitor is administered in a dosage of about 5-20 mg/day (see sec under method –highlighted) as in claim 6, wherein the said chronic heart failure is asymptomatic left ventricular systolic dysfunction (see sec under method –highlighted) as in claims 3 and 4) having an impaired fasting plasma glucose (see page 1292-sec data collection) as in claim 2.

Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Yusuf et al. JAMA 2001;286(15);1882-1885 (submitted by Applicant).

The above reference teaches ACE inhibitor ramipril reduces myocardial infarction such as strokes, death in the development of nephropathy-(see page 1882 first col. and mid sec of 2nd col.) thus diabetic nephropathy is kidney disease that develops as a

result of diabetes mellitus (DM) and chronic heart failure (myocardial infarction) occurs when an area of heart muscle dies or is permanently damaged because of an inadequate supply of oxygen to that area as in the instant claims 1, and 5, wherein the ace inhibitor is is administered in a dosage of 10 mgper day (see page 1883 line 10) as in claim 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. Amer. Heart J. 138(5, part 1):849-855 taken with Bauters et al. Cardiovascular Diabetology , 2003, 2:1 pages 1-16 and Pan et al. US 5130333.

The above reference teaches with regards to the instant claim 1, administering ACE inhibitors to patients in order to reduce renal function in patients, diabetes is associated with an increased risk of renal impairment in patients with chronic heart failure, but the risk was reduced when an ACE inhibitor enalpril was administered as in claims 1, 5 and 7 (see conclusion-highlighted). (Diabetes is a generic term for the different types of diabetes-therefor diabetes mellitus is inclussive).

The Bauters et al. reference teaches the said chronic failure (CHF) is a result of left ventricular systolic dysfunction (see page 5, lft.col first para. highlighted sec) as in claims 3 and 4, wherein the subject has impaired fasting plasma glucose (see page 5, lft.col 2nd para. highlighted sec) as in claim 2, wherein the drug is an ACE inhibitor – enalapril as in claims 1 and 7.

Pan et al teach administering enalapril in a dosage of 0.1-500 mg to patients with diabetes mellitus (see col. 11, lines 66-68 and col. 12 lines 1-2) once a day (see col. 12, lines 28-29).

One of ordinary skill in the art would have been motivated to combine the above cited art administer enalapril an ACE inhibitor to inhibit the incidence of diabetes mellitus in a subject with chronic heart failure because the prior art teaches so and has been shown that diabetes mellitus is prevalent in heart failures as taught by Bauters et al. (see abstract) and one would have been motivated to administer the drug in the range of 5 mg-20 mg per day as taught by Pan et al. (see col. 12, line 1).

The motivation comes from the teachings as the teaching teach by Knight et al. wherein Ace inhibitors are administered to patients to reduce renal function in patients with an increased risk of CHF.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
3/7/07

Ardin H Marschel 3/17/07
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SUPERVISORY PATENT EXAMINER